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## **Patients with chronic obstructive pulmonary disease in rehabilitation**

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## Summary

For patients with chronic obstructive pulmonary disease (COPD) living with its symptoms and consequences is a burden. Many patients experience breathlessness or dyspnea, fatigue and reduced exercise tolerance. Living with these symptoms can be distressing and may result in sensations of anxiety and depression. Moreover, it can trigger, or be accompanied by pre-existing, psychological symptoms. These psychological symptoms can interfere with adequate disease management, treatment adherence maintaining a healthy life style.

This thesis addresses the prevalence and impact of psychological symptoms in patients with COPD who are referred for pulmonary rehabilitation. In the first chapter, the aims of this thesis are introduced and an outline is presented. The association between COPD and psychological symptoms has received relative little attention from the field of health-psychology researchers as well as from medical researchers, in comparison to research in other medical conditions such as cardiovascular diseases. Quality of life research and the development of disease specific assessment instruments inspired pulmonary physicians to be more sensitive to the role of subjective symptoms in addition to objective measures. Elevated subjective symptoms are often an indicator for referral for pulmonary rehabilitation.

Evidence based support for pulmonary rehabilitation has grown enormously. Pulmonary rehabilitation reduces dyspnea, increases exercise capacity and both physical and social activities and improves health related quality of life. No longer is pulmonary rehabilitation seen as a desperate effort in the management for patients with severe COPD. Currently, pulmonary rehabilitation should be an integral part of the management of all patients with chronic respiratory conditions.

Pulmonary rehabilitation comprises mostly of exercise training, nutritional intervention, psychosocial support and patient education. The contents of these components vary from time to time, from facility to facility and from country to country due to differences in resources, health insurance systems, inclusion criteria and advances in understanding of the pathology of chronic respiratory conditions.

In chapter 2, an overview of pulmonary rehabilitation at the Center for Rehabilitation (CVR) of the University Medical Center of Groningen (UMCG) is given. Pulmonary rehabilitation is offered to patients on an inpatient as well as an outpatient basis. Patients are referred for pulmonary rehabilitation by lung physicians. Common reasons for referral are multiple hospitalizations, anxiety engaging activities, dyspnea and limitations in basic and social activities due to respiratory impairment. All patients are assessed on lung function, exercise

capacity, muscle strength, nutritional status and both psychological state and trait variables. After which an appropriate plan of care is presented.

Aforemost component of pulmonary rehabilitation is exercise training consisting of one or more specific modules, including desensitization, resistance training, endurance training, weight loss exercise training, inspiratory muscle training and breathing strategy training.

When indicated, interventions to treat body composition abnormalities are provided. Special attention is given to patients with a low body mass index (BMI) or fat free mass index (FFMI) or to patients with obesity. Interventions may consist of caloric supplementation and exercise training in case of patients with a low BMI or nutritional education, restricted calorie intake, exercise training and psychological support in case of obese patients.

Also, patient education is an important component of pulmonary rehabilitation and it provides patients with information with reference to the disease and therapy. Self-management is the central idea in patient education, thus increasing patient's self efficacy and capabilities in taking responsibility for health and lifestyle.

The results on the self-report questionnaires that are used for screening for psychological symptoms such as anxiety and depression symptoms, next to coping strategies and personality characteristics are indicative for further psychological assessment and possible treatment. Many patients report elevated anxiety and depression symptoms and are treated mostly with cognitive behavioral therapy and occasionally antidepressants. Patients with severe psychiatric disorders or alcohol or drug abuse are referred for specialist care.

Compared to the international guidelines proposed by the ATS/ERS, the components of pulmonary rehabilitation at the UMCG are generally in line with these evidence based recommendations. Standard outcome measurement is the single point the CVR should improve on.

In chapter 3, the aim was to examine the prevalence of common psychological symptoms and common personality characteristics in patients with COPD referred for pulmonary rehabilitation and compare them with normative data. Next, the association between psychological symptoms and background and biomedical data, including BMI, FFMI, lung function and exercise capacity, was studied.

All the data was collected during standard care. Upon admission, demographic data, such as sex, age, educational level, marital status and smoking behavior were registered. Also, in the initial week of the pulmonary rehabilitation, patients were assessed on lung function, exercise capacity, nutritional status and psychological symptoms and personality characteristics. In this study, most patients were male and all patients had moderate to severe COPD.

With regard to psychological symptoms, both male and female patients reported higher scores on all psychological symptom dimensions, except for interpersonal sensitivity and feelings of hostility, in comparison with 'normal' controls. In comparison with an out-patient psychiatric population, all patients with COPD reported lower scores on all psychological symptom dimensions. A remarkable result was that patients with COPD in our study reported to have a lower self esteem, to be less rigid, and to be more distrustful, irritable and less altruistic in comparison with normative data from the general population and with normative data from somatic patients reference groups.

A common held belief is that psychological symptoms in patients with COPD co-vary with biomedical data such as lung function or exercise capacity. In our study sample, almost all psychological markers, both psychological symptoms and personality characteristics, did not co-vary with biomedical variables. Only the personality characteristic extraversion was weakly but consistently associated with patient's physical condition. The poorer the condition the less extravert the patient reports to be. We concluded that screening for psychological impairments should be integrated in the standard care for patients with COPD.

In the next chapter (chapter 4), we examined the prevalence of anxiety and depression symptoms in patients with COPD in rehabilitation and compare them with population samples of pulmonary patients and healthy subjects. Several studies have demonstrated that anxiety and depression symptoms are common in patients with COPD. However, they often go unrecognized and untreated. This is remarkable because anxiety and depression symptoms are associated with poor medication compliance, hospital admission, and relapse after treatment and early withdrawal from rehabilitations programs. High levels of anxiety and depression symptoms, (up to 30 %) were found in our study sample and in the population sample of pulmonary patients, whereas similar levels of anxiety and depression symptoms were less prevalent (ca 10%) in healthy subjects. Anxiety symptoms were more prevalent in female patients and in patients without a partner. Depression symptoms were more prevalent in lower educated patients than in higher educated patients. Based on these findings we recommend adequate assessment of anxiety and depression symptoms in pulmonary patients irrespective of the setting of treatment, in order to provide timely treatment and follow-up of these symptoms when necessary.

After having established the high prevalence of anxiety symptoms in our study sample, we examined the relationship between anxiety and dyspnea on exertion in the next chapter (chapter 5). Dyspnea is one of the characteristic symptoms of COPD. It limits exercise, consequently influencing functional capacity and quality of life. Borg scores are used to assess dyspnea and

fatigue in patients during incremental cycle ergometry while they are actually experiencing dyspnea. Therefore, these Borg scores are less sensitive to factors such as emotional and motivational states which may interfere with recall of symptoms. Several studies in COPD have demonstrated that more dyspnea leads to higher anxiety. Nonetheless, the inverse relation, whether anxiety is independently associated with dyspnea on exertion may well be apparent to clinicians but studies on this matter are scarce.

In this study, we demonstrated that in patients with clinically stable COPD anxiety was associated with dyspnea on exertion, adjusted for sex, age and baseline dyspnea and exercise capacity. The total variance of Borg scores of dyspnea on exertion was only partly explained by the predictor variables in our model, leaving most variance unexplained. However, our findings could have interesting implications. Not only could results of exercise training be negatively influenced by anxiety worsened dyspnea but also activities in daily life may be influenced by this mechanism. Our results give support to the hypothesis that dyspnea have both sensory and affective dimensions. It is the affective dimension of perceived dyspnea that is vulnerable to emotional states such as anxiety. Further research to disentangle the complexity of dyspnea on exertion and its sensory and affective components is encouraged. The next two studies, (chapters 6 and 7), deal with a topic that is gaining interest in the last decade; mortality. COPD is expected to become the third most frequent cause of death by the year 2020. Most studies on predictors of mortality in COPD have mainly focused on physiological variables. Only a few studies examined the impact of depression in COPD patients hospitalized for exacerbation. However, little is known whether depression symptoms predict mortality in clinically stable patients with COPD. Depression symptoms are known to be predictors of mortality in other medical conditions including cardiovascular disease and diabetes. Moreover, depression symptoms are common in COPD. We examined the association between depression symptoms and mortality in clinically stable COPD patients in two separate studies.

In the first study (chapter 6), depression was assessed with the Beck's Depression Inventory (BDI) and in the second study (chapter 7) depression was assessed with the depression scale of the Hospital Anxiety and Depression scale (HADS). Both studies had a long term follow-up, 8.5 years in the first study and 6 years in the second study. In both studies, depression symptoms were found to be independently associated with higher mortality. Two possible pathways are discussed; the hypothalamic pituitary adrenal (HPA) axis functioning and the behavioral mechanism of low self-care, apathy, avoidance of exercise and low treatment adherence leading to worsening of the physical condition and death eventually. Our finding that depression symptoms are

associated with mortality does not imply a causal relationship. Most likely an unmeasured confound could be at play in this relationship. We hypothesize general disease burden or misery is a good candidate.

In cardiovascular disease, the distressed personality (Type D) offered an explanation for the association between depression and mortality. In our second study (chapter 7), we examined if Type D offers an explanation to our observed relation in stable COPD patients. Type D was associated with depressive symptoms in our study sample. However, Type D was as prevalent in COPD patients that died as it was in patients that survived. So, we concluded that Type D was not a prognostic factor for mortality in COPD. In both studies, we discussed that exploring trajectory and stability over time of depressive symptoms and studying specific components of depressive symptoms are good steps for future research.

In the final chapter, (chapter 8), our main findings are presented and discussed with regard to implications for clinical practice and research. Studies presented in this thesis clearly demonstrate the high prevalence of psychological symptoms and that they are not merely surrogates for vegetative symptoms. Therefore, patients with COPD should be screened for psychological symptoms so adequate treatment could be provided to them when indicated. Also, clinicians working in pulmonary rehabilitation may benefit from our findings. In patient selection, screening for psychological symptoms and subsequently addressing them when indicated, favor outcomes of pulmonary rehabilitation. Patients may benefit from anxiety reducing exercises or cognitive behavioral therapy before commencing physical exercises that trigger unpleasant sensations including dyspnea and anxiety. Or, when patients report substantial depressive symptoms, healthcare professionals should look for its determinants and provide adequate care in order to improve patient's quality of life and reduce poor medication compliance or continued smoking.

Regularly, results give few answers but raise many questions. For instance, etiology, determinants, stability and trajectory over time of psychological symptoms and their subsequent association with COPD symptoms and prognosis, need to be explored further. Interventions to improve patient's quality of life and reduce disease burden should be evaluated and innovated, including relapse prevention strategies.